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Copyright (c) 2009 The Thomson Corporation

=> HCV (L) core

L1 4507 HCV (L) CORE

=> aluminum (L) adjuvant

L2 2263 ALUMINUM (L) ADJUVANT

=> L1 and L2

L3 6 L1 AND L2

=> ISCOM

L4 1094 ISCOM

=> L1 and L4

L5 4 L1 AND L4

=> D L5 THIS ABS 1-4

L5 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN



ACCESSION NUMBER: 2004:997248 CAPLUS  
 TITLE: Hepatitis C vaccines to prevent liver cancer  
 AUTHOR(S): Houghton, M.  
 CORPORATE SOURCE: Chiron Corporation, Emeryville, CA, USA  
 SOURCE: Developments in Biologicals (Basel, Switzerland)  
 (2004), 116(Development of Therapeutic Cancer  
 Vaccines), 191-192  
 CODEN: DBEIAI; ISSN: 1424-6074  
 PUBLISHER: S. Karger AG  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The hepatitis C virus (**HCV**) infects ~ 170 million individuals world-wide with a substantial annual incidence of new infections. At least 50% of infections become persistent and while most are relatively asymptomatic, there is a significant risk of a sequential progression to chronic active hepatitis, liver cirrhosis and then hepatocellular carcinoma (HCC). In Japan, **HCV** is the major risk factor for HCC. In essentially all cases, HCC is preceded by liver cirrhosis indicating that the latter is an abs. requirement for **HCV**-assocd. liver cancer development. Various viral factors have also been postulated to be

directly involved. Possible approaches to preventing **HCV**-related HCC include the development of a prophylactic vaccine to prevent the development of persistent infection following virus exposure, as well as therapeutic vaccines to either slow the progression of liver disease or to eradicate viral infection through the boosting of viral-specific humoral and cellular immune responses. Since the outcome of the std.-of-care treatment for chronic **HCV** patients (a combination of interferon-alpha and the guanosine analog ribavirin) appears to be dependent in part on the quality and quantity of both **HCV**-specific humoral and cellular immune responses, a therapeutic vaccine may be most effective when used as an adjunct with these and future antiviral drugs. A prophylactic vaccine comprising recombinant envelope glycoproteins E1 and E2 has been shown to prevent the development of persistent infection following exptl. challenge with both homologous and heterologous viral inocula in vaccinated chimpanzees, which represent the only animal model available. A related vaccine formulation is about to enter clin. trials in the USA. This vaccine primes the induction of anti-envelope antibodies as well as CD4+ T helper responses and may also be of value in treating chronically-infected patients with liver disease. In addn., we have been investigating methods to prime and boost **HCV**-specific cytotoxic lymphocytes (CTLs) capable of killing infected hepatocytes as well as secreting antiviral cytokines which are therefore of potential therapeutic value. One effective method is the combination of the **ISCOMs** adjuvant (CSL Ltd) with a variety of recombinant **HCV** proteins. In rhesus macaques, a **core** protein adjuvanted with **ISCOMs** was shown to be very effective at priming **core**-specific Th1-like CD4+ T cells as well as CD8+ CTLs. Recently, this work has been extended to a large yeast-derived **HCV** polyprotein comprising the nonstructural proteins 3, 4 & 5 fused to the **core** protein. When adjuvanted with **ISCOMs**, strong multispecific T helper and CTL responses have been elicited in vaccinated chimpanzees that were superior to those elicited by various **HCV** DNA vaccine formulations.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN



ACCESSION NUMBER: 2004:392569 CAPLUS  
DOCUMENT NUMBER: 140:390291  
TITLE: Activation of HCV-specific T cells using fusion protein vaccines comprising HCV NS3, NS4, NS5a, and NS5b polypeptides  
INVENTOR(S): Houghton, Michael; Coates, Steve; Selby, Mark; Paliard, Xavier  
PATENT ASSIGNEE(S): Chiron Corporation, USA  
SOURCE: PCT Int. Appl., 136 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039950	A2	20040513	WO 2003-US33610	20031024
WO 2004039950	A3	20071122		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,

OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,  
 TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY,  
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 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG,  
 AP, EA, EP, OA

CA 2505611 A1 20040513 CA 2003-2505611 20031024  
 AU 2003287188 A1 20040525 AU 2003-287188 20031024  
 EP 1576125 A2 20050921 EP 2003-781368 20031024

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.:

US 2002-281341 A 20021025  
 WO 2003-US33610 W 20031024

AB The invention provides a method of activating hepatitis C virus  
 (HCV)-specific T cells, including CD4+ and CD8+ T cells. HCV-specific T  
 cells are activated using fusion protein vaccines comprising HCV NS3, NS4,  
 NS5a, and NS5b polypeptides, polynucleotides encoding such fusion  
 proteins, or polypeptide or polynucleotide compns. contg. the individual  
 components of these fusions. The method can be used in model systems to  
 develop HCV-specific immunogenic compns., as well as to immunize a mammal  
 against HCV.

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN



ACCESSION NUMBER: 2001:396697 CAPLUS  
 DOCUMENT NUMBER: 135:4467  
 TITLE: Vaccine compositions  
 INVENTOR(S): Drane, Debbie; Cox, John; Houghton, Michael; Paliard,  
 Xavier  
 PATENT ASSIGNEE(S): Csl Limited, Australia; Chiron Corporation  
 SOURCE: PCT Int. Appl., 67 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037869	A1	20010531	WO 2000-AU1410	20001117
WO 2001037869	A9	20020718		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,			
	CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,			
	HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,			
	LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,			
	SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,			
	ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,			
	DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,			
	BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2391843	A1	20010531	CA 2000-2391843	20001117
AU 2001013730	A	20010604	AU 2001-13730	20001117
AU 772617	B2	20040506		
EP 1239876	A1	20020918	EP 2000-975681	20001117
EP 1239876	B1	20080730		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
NZ 518999	A	20021220	NZ 2000-518999	20001117

JP 2003514872	T	20030422	JP 2001-539483	20001117
NZ 520976	A	20050128	NZ 2000-520976	20001117
AT 402715	T	20080815	AT 2000-975681	20001117
ES 2311478	T3	20090216	ES 2000-975681	20001117
ZA 2002003986	A	20031217	ZA 2002-3986	20020520
KR 875483	B1	20081222	KR 2002-706431	20020520
HK 1047892	A1	20090109	HK 2003-100096	20030103
US 20040191270	A1	20040930	US 2003-622470	20030721
PRIORITY APPLN. INFO.:			US 1999-166652P	P 19991119
			US 2000-224362P	P 20000811
			US 2000-714438	B1 20001117
			WO 2000-AU1410	W 20001117

AB The present invention relates generally to an immunogenic complex comprising a charged org. carrier and a charged antigen and, more particularly, a neg. charged org. carrier and a pos. charged antigen, wherein the charged antigen is a polyprotein of Hepatitis C Virus (**HCV**), particularly the **core** protein of **HCV**, or a fragment thereof, or a fusion protein comprising the polyprotein or a fragment thereof. The complexes of the present invention are useful in vaccine compns. as therapeutic and/or prophylactic agents for facilitating the induction of immune responses, and in particular a cytotoxic T-lymphocyte response, in the treatment of a disease condition which results from an **HCV** infection.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN



ACCESSION NUMBER: 2001:167132 CAPLUS  
DOCUMENT NUMBER: 134:324893  
TITLE: Characterization of hepatitis C virus core-specific immune responses primed in rhesus macaques by a nonclassical **ISCOM** vaccine  
AUTHOR(S): Polakos, Noelle K.; Drane, Debbie; Cox, John; Ng, Philip; Selby, Mark J.; Chien, David; O'Hagan, Derek T.; Houghton, Michael; Paliard, Xavier  
CORPORATE SOURCE: Chiron Corp., Emeryville, CA, 94608, USA  
SOURCE: Journal of Immunology (2001), 166(5), 3589-3598  
CODEN: JOIMA3; ISSN: 0022-1767  
PUBLISHER: American Association of Immunologists  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Current therapies for the treatment of hepatitis C virus (**HCV**) infection are only effective in a restricted no. of patients. Cellular immune responses, particularly those mediated by CD8+ CTLs, are thought to play a role in the control of infection and the response to antiviral therapies. Because the **Core** protein is the most conserved **HCV** protein among genotypes, the authors evaluated the ability of a **Core** prototype vaccine to prime cellular immune responses in rhesus macaques. Since there are serious concerns about using a genetic vaccine encoding for **Core**, this vaccine was a non-classical **ISCOM** formulation in which the **Core** protein was adsorbed onto (not entrapped within) the ISCOMATRIX, resulting in ~1-µm particulates (as opposed to 40 nm for classical **ISCOM** formulations). The authors report that this **Core-ISCOM** prototype vaccine primed strong CD4+ and CD8+ T cell responses. Using intracellular staining for cytokines, the authors show that in immunized animals 0.30-0.71 and 0.32-2.21% of the circulating CD8+ and CD4+ T cells, resp., were specific for naturally processed **HCV Core** peptides. Furthermore, this vaccine elicited a Th0-type response and induced a high titer of Abs against **Core** and long-lived cellular immune responses. Finally, the

authors provide evidence that **Core-ISC** could serve as an adjuvant for the **HCV** envelope protein E1E2. Thus, these data provide evidence that **Core-ISC** is effective at inducing cellular and humoral immune responses in nonhuman primates.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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